UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/469,485	12/22/1999	QINJIAN ZHAO	20369Y	5022

210 7590 12/03/2002

MERCK AND CO INC
P O BOX 2000
RAHWAY, NJ 070650907

EXAMINER
FOLEY, SHANON A

ART UNIT	PAPER NUMBER
1648	12

DATE MAILED: 12/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/469,485	ZHAO ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

In paper no. 10, applicant amended claims 8, 14 and 19. Claims 1-20 are pending, claims 1-7 are withdrawn due to non-elected subject matter and claims 8-20 are under consideration.

The double patenting rejection is obviated since 09/869007 has been abandoned.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record.

Applicant states that there is antecedent basis for step d) since claim 20 ultimately depends from claim 8. However, this is found unpersuasive because claim 20 depends directly from claim 17, which does not mention step d). Therefore, there remains a lack of antecedent basis for this step.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 8 has been amended to recite "soluble" rHBsAg. Applicant states that support for the amendment is found on pages 7-8 and example 1. However, after a careful review of the passages cited by applicant, it is determined that support for this amendment cannot be found. Page 7, line 32 to page 8, line 6, states that the redox step is followed after the protein is purified from a cellular system and discusses the teachings of Wampler et al. as a prior art example for obtaining rHBsAg. The sample in example 1 on page 19, lines 10-12, is indicated to have been purified by the method taught by Wampler et al. However, there is no indication that the rHBsAg is soluble or required to be soluble to practice the invention. Although Wampler et al. may have used soluble antigen, the teachings of Builder et al. indicate that rHBsAg may also be present in insoluble form from cultured cells. Therefore, since it is known in the art that rHBsAg may exist in soluble and insoluble forms and there is no teaching in the disclosure that would indicate that only soluble forms of the antigen are used to practice the invention, it is determined that the amendment presents new matter into the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 8-16 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable Builder et al. (US 4,620,948) for reasons of record.

Applicant argues that Builder et al. does not render the instant invention obvious because Builder et al. is concerned with eliminating refractile bodies and the instant invention uses

soluble antigen. Therefore, applicant concludes that there since there are no refractile bodies present in the instant invention, the ordinary artisan would not be motivated to use the method taught by Builder et al.

Applicant's arguments have been fully considered, but are found unpersuasive because it has been determined that the "soluble" limitation is new matter for reasons discussed above.

However, even if the protein is soluble, it is maintained that the invention would have been prima facie obvious to the skilled artisan in view if the teachings of Builder et al. Although the focus of Builder et al. is on recovering protein from refractile bodies, the reference discusses misfolding of proteins that occurs within the cell culture or isolation conditions or both. The reference emphasizes the importance of correct disulfide bond formation to obtain a biologically active protein, which is obtained by adding 10mM GSH: 1mM GSSG and incubating the mixture overnight at 37°C, see column 3, lines 34-68, examples 13 and 14 and column 16, lines 29-55. Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to correct misfolding that may have occurred during cell culture and/or isolation to obtain a biologically active protein. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing the instant invention because Builder et al. teaches refolding solubilized protein in weaker denaturants and a sulfhydryl compound, see column 5, lines 3-9 for example. Therefore, it is maintained that the invention would be prima facie obvious for reasons of record.

Claims 17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Builder et al. as applied to claims 8-16 and 20 above, and further in view of Petre et al. (WO 93/24148 A1) for reasons of record.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Builder et al. as applied to claims 8-16 and 20 above, and further in view of Even-Chen (US 5,242,812) for reasons of record.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley
November 29, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600